

wherein Y comprises a carboxyl group or an amino acid sequence which is not derived from NS5B.

20. (New) The polypeptide of claim 19, wherein the C-terminal amino acid residue of X is an amino acid residue selected from the group consisting of 536 (Leu) to 552 (Val) of the NS5B.

21. (New) The polypeptide of claim 20, wherein the C-terminal amino acid residue of X is an amino acid residue selected from the group consisting of 536 (Leu) to 544 (Gln) of the NS5B.

22. (New) The polypeptide of claim 20, wherein the C-terminal amino acid residue of X is an amino acid residue selected from the group consisting of 531 (Lys) to 544 (Gln) of the NS5B.

23. (New) The polypeptide of claim 19, wherein methionine residues in the amino acid sequence of X are replaced by selenomethionine residues.

24. (New) The polypeptide of claim 19, wherein Y is an amino acid sequence not derived from NS5B, and said amino acid sequence is suitable for column purification.

25. (New) The polypeptide of claim 19, wherein the NS5B comprises an amino acid sequence of SEQ ID NO: 1.

26. (New) The polypeptide of claim 19, wherein said polypeptide is identified by three-dimensional structural coordinates shown in a table selected from the group consisting of Table 2 and Table 3.

27. (New) A crystal comprising the polypeptide of claim 19.

28. (New) A DNA encoding the polypeptide of claim 19.

29. (New) A method for determining three-dimensional structural coordinates of a variant of HCV polymerase NS5B by the molecular replacement method using a three-dimensional structure coordinate of said NS5B.

30. (New) A method for designing or identifying HCV polymerase inhibitors, which comprises determining the complementarity of a test compound with an active site and/or RNA binding cleft of a polypeptide using the three-dimensional structural coordinate of said polypeptide or its part and the three-dimensional structural coordinate of the test compound, wherein said polypeptide is derived from the HCV polymerase NS5B having an HCV polymerase activity and consisting of an amino acid sequence X-Y, wherein X is a consecutive amino acid sequence which is a portion of the NS5B, an N-terminal amino acid of X is the amino acid residue 1 (Ser) of the NS5B, a C-terminal amino acid residue of X is any one of amino acid residues 531(Lys) to 570 (Arg) of the NS5B; and

wherein Y is a carboxyl group or another amino acid sequence which is not derived from NS5B; and one or more amino acids in X may be modified, and methionine residues in the amino acid sequence of X may be replaced by selenomethionine residues.

31. (New) A method for designing or identifying HCV polymerase inhibitors, which comprises the steps of:

(a) determining the complementarity of a test compound with an active site and/or RNA binding cleft of a polypeptide using a three-dimensional structural coordinate of said polypeptide or its part and a three-dimensional structural coordinate of said test compound, wherein said polypeptide is derived from the HCV polymerase NS5B having an HCV polymerase activity and consisting of an amino acid sequence X-Y, wherein X is a consecutive amino acid sequence which is a portion of the NS5B, an N-terminal amino acid of X is the amino acid residue 1 (Ser) of the NS5B, a C-terminal amino acid residue of X is any one of amino acid residues 531 (Lys) to 570 (Arg) of the NS5B; and

wherein Y is a carboxyl group of another amino acid sequence which is not derived from NS5B; and one or more amino acids in X may be modified, and methionine residues in the amino acid sequence of X may be replaced by selenomethionine residues;

(b) determining HCV polymerase-inhibitory activity of said test compound; and
(c) designing or determining HCV polymerase inhibitors using the complementarity data of said test compound determined in the above (a), and the inhibitory activity data obtained in the above (b).

32. (New) The method of claim 29, wherein the three-dimensional structural coordinate of the polypeptide is selected from the group consisting of dimensional structural coordinates shown in a table selected from the group consisting of Table 2 and Table 3.

33. (New) A method for identifying HCV polymerase inhibitors, which comprises the steps of:

- (a) obtaining a polypeptide, which is derived from the HCV polymerase NS5B has an HCV polymerase activity, and consisting of the amino acid sequence X'-Y, wherein X' is a consecutive amino acid sequence which is a portion of the NS5B, an N-terminal amino acid of X' is the amino acid residue 1 (Ser) of the NS5B, a C-terminal amino acid residue of X' is any one of amino acid residues 531 (Lys) to 544 (Gln) of the NS5B; and wherein Y is a carboxyl group or another amino acid sequence which is not derived from NS5B; and one or more amino acids in X' may be modified, and methionine residues in the amino acid sequence of X' may be replaced by selenomethionine residues;
- (b) determining the HCV polymerase activity of said polypeptide by reacting said polypeptide obtained in the above (a) with a template RNA and substrates in the presence of a test compound;
- (c) determining the HCV polymerase activity of said polypeptide by reacting polypeptide obtained in the above (a) with a template RNA and substrates in the absence of said test compound; and
- (d) comparing the HCV polymerase activity of the above (b) with the HCV polymerase activity of the above (c).

34. (New) An HCV polymerase inhibitor, identified by the method of claim 30.

35. (New) An HCV polymerase inhibitor that inhibits the HCV polymerase activity of HCV polymerase NS5B by acting on a boundary between Thumb and Palm domains of NS5B.

36. (New) The HCV polymerase inhibitor of claim 35, wherein said inhibitor is a compound represented by the formula, Z-Asp-Leu-Ser-Gly-Trp-Phe-Z', wherein Z is Leu or a hydrophilic group, and Z' is Val or a hydrophilic group.

REMARKS

Claims 19-36 are now pending in this application and are supported in originally pending, now canceled claims 1-18. No new matter has been added.